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Title

Tear dynamics under scleral lenses.

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<https://escholarship.org/uc/item/7z24n2k6>

Journal

Contact lens & anterior eye : the journal of the British Contact Lens Association, 42(1)

ISSN

1367-0484

Authors

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et al.

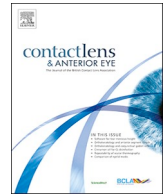
Publication Date

2019-02-01

DOI

10.1016/j.clae.2018.11.016

Peer reviewed



Tear dynamics under scleral lenses

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ARTICLE INFO

Keywords:

Scleral lens
Tear exchange
Tear mixing
Fluorescence intensity
Fluorogram
OCT

ABSTRACT

Purpose: To evaluate post-lens tear dynamics at two different time points during scleral lens wear in two cohorts with 10 neophytes each.

Methods: All subjects wore bilaterally scleral lenses for 5 h on 3 separate visits. Post-lens tear exchange was measured using Out-in method, which required 5 μ L of 2% FITC-Dextran instilled on the bulbar conjunctiva during lens wear. Time taken to observe the first sign of fluorescence in post-lens tear reservoir was recorded with a stopwatch. Out-in measurements were collected at 5-hour post-lens insertion in Group 1 and compared with those obtained at 20 min of lens wear in Group 2. Tear dynamics under the lens was observed in Group 2 with fluorogram using a modified slit-lamp technique (Tan et al., 2018) to monitor post-lens fluorescence intensity and with high-resolution spectral domain optical coherence tomography (ENVISU 2300; Biophtigen Inc.) to measure post-lens tear thickness (PoLTT) over 5 h of lens wear.

Results: 60% of subjects in Group 1 achieved Out-in times less than 5 min at 5-hour post-lens insertion, compared with 67% of subjects at 20-min lens wear (Tan et al., 2018). Using qualitative analysis on 60 series of data in Group 2 to compare the changes in fluorescence intensity and PoLTT with respect to lens-wearing time, 27% was due to lens settling, 13% was due to tear exchange and mixing while 60% indicated tear dynamics under scleral lenses was due to a combination of tear exchange, mixing, and lens settling.

Conclusion: Tear flow into tear reservoir under a scleral lens on subjects with healthy cornea occurred at 20 min and 5 h after lens insertion. After 5 h of lens wear, roughly one third of the subjects had no tear flow into post-lens reservoir, as the observed decline in post-lens tear fluorescence was predominately due to lens settling.

1. Introduction

Efficient tear exchange and mixing are important during contact lens wear because they facilitate the clearance of trapped debris, inflammatory cells, and metabolic by-products that accumulate underneath the contact lens and also help preserve ocular surface integrity by delivering oxygenated tears to the cornea [1–3]. Previous studies have thoroughly investigated tear exchange and mixing on corneal gas-permeable lens and soft contact lens. Corneal gas-permeable lens has a faster tear exchange rate than soft contact lens [1,2,4–6]. Efficient removal of trapped debris minimizes biomechanical and biophysical effects on corneal epithelial surface and possibly reduces the risk of infection or inflammation on the ocular surface under a corneal gas-permeable lens [4,5]. Tear dynamics under a soft contact lens is mostly influenced by the transverse (in-out) and vertical (up-down) lens motions that occur while blinking over a soft contact lens [1]. A soft contact lens made with higher modulus material can increase the

transverse lens motion and cause more efficient tear exchange [1]. Because of the combination of a thin post-lens tear film and slower tear exchange [7–9], the back surface of a soft contact lens along with accumulated unwanted substances agitate against the corneal epithelial surface and leads to adverse events and contact lens-induced complications [3,10,11].

As scleral lens wear is regaining popularity in recent years, tear exchange and mixing with scleral lenses have drawn more attention. Unlike corneal gas-permeable lenses and soft contact lenses, where tear-exchange dynamics predominantly controls tear mixing to allow synonymous usage of the two terms [12], tear exchange and tear mixing first must be redefined for scleral lens wear due to its unique on-eye lens dynamics. Tear exchange is defined as tear flow between the tears uncovered by a scleral lens and the post-lens tear reservoir. Tear mixing, which may occur without tear exchange, occurs within the tear reservoir underneath a scleral lens [9].

Tan et al. [13] showed slow post-lens fluorescence decay with

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<https://doi.org/10.1016/j.clae.2018.11.016>

Received 30 June 2018; Received in revised form 17 November 2018; Accepted 28 November 2018

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scleral lens wear. However, this fluorescence decay could not relate directly to tear exchange or mixing with scleral lens due to combined result of post-lens tear-film thinning and fluorescein concentration reduction. Scleral lens has been observed to settle quickly during the first two hours after lens insertion and continued to settle through the 5-hour lens wear period [13–15]. Post-lens tear-film thinning was caused by lens settling, while fluorescein concentration reduction was caused by tear exchange and mixing. However, it remains unclear what the relative contributions are from lens settling and tear exchange in resulting fluorescence decay in the post-lens tear film. To further understand tear flow dynamics with scleral lenses, post-lens tear exchange was compared at two different time points of lens wear, using the Out-in method [13]. Fluorogram with a modified slit-lamp technique [13,16] was also utilized to assess the tear dynamics underneath the scleral lenses while monitoring lens-settling measurements.

2. Methods

2.1. Study design

This was a prospective, double-masked, randomized, bilateral, crossover, single-center (University of California, Berkeley, Clinical Research Center) study involving four visits. This research project adhered to the tenets of the Declaration of Helsinki; it was approved by institutional review board (Committee for Protection of Human Subjects, University of California, Berkeley) and was compliant with the Health Insurance Portability and Accountability Act.

2.2. Subjects

Neophytes (with no prior history of contact lens wear or no contact lens wear for at least one year prior to enrollment) were recruited from the University of California, Berkeley campus and the surrounding community. Eligibility criteria included age greater than 18 years old, a self-report eye examination in the last two years, spectacle spherical prescription between -0.25 to -8.00 D, corrected visual acuity of 20/30 or better in each eye with habitual spectacles, and healthy ocular surface (i.e., free of ocular pathology including moderate to severe dry eyes). A questionnaire was administered at the screening visit to collect demographic information, ocular health history, and medical history pertaining to ocular and system illnesses, and use of medications.

This study involved 2 separate cohorts with 4 visits each. At the first visit, each subject read and signed an informed consent, followed by a screening exam of the ocular surface and scleral lens fitting. Baseline visual acuity was measured, corneal topography was taken (Medmont E300 Medmont International Pty Ltd, Vermont, Australia), and ocular-surface health was assessed using slit-lamp biomicroscopy (SL120, Carl Zeiss Meditec Inc., Jena, Germany) with sodium fluorescein (BioGlo™ Fluorescein Strips, HUB Pharmaceuticals, LLC, Rancho Cucamonga, CA). Based on corneal sagittal heights, keratometry readings, and elevation maps generated by Medmont topography, all qualified subjects were fitted bilaterally with Essilor Jupiter Scleral Lens standard lens design (Essilor USA, Dallas, TX) to determine appropriate lens parameters for acceptable lens fits. After 20–30 min of lens settling, over-refraction and lens assessment were performed and post-lens tear thickness (PoLTT) was measured using high-resolution spectral domain optical coherence tomography (ENVSISU 2300, Biotigen Inc, Durham NC). Based on these measurements, the appropriate lenses were ordered for three subsequent visits for each group. For Group 1, the lenses with similar lens fit (i.e. a fit with ~ 100 – 250 μ m central tear clearance) with various lens oxygen permeability values (100, 140, and 160 Dk) were ordered. For Group 2, the lenses with three different fits (an ideal fit of ~ 200 – 250 μ m tear clearance; a steep fit of ~ 400 – 500 μ m tear clearance; and a flat fit of ~ 100 – 150 μ m tear clearance) in the same lens material (97 Dk) were ordered.

For Visits 2–4, appointment times were kept the same (± 30 min)

with each subject arriving at least 2 h after awakening and with discontinuation of eye drops or allergy medications one full day before the visit. Baseline visual acuity was measured and ocular-surface health was assessed with slit-lamp biomicroscopy. The investigator then inserted one of three different pairs of scleral lenses, according to pre-determined randomization schemes. It was important to ensure all lens fits were acceptable with appropriate peripheral curves because tear exchange was being evaluated for both groups. Then visual acuity with scleral lenses was measured and over-refraction was performed. Tear exchange near the lens periphery was assessed by measuring the Out-in time at 5-hour post-lens insertion for Group 1. 5 μ L of 2% w/v FITC-Dextran solution (Molecular weight (MW) = 10,000D) was instilled using a micropipette on the central area of the superior bulbar conjunctiva of the subject's eye as the subject was instructed to look down. The subject's post-lens tear film was monitored for the first sign of fluorescence with the slit-lamp biomicroscope set at a 16–20 magnification with an optic section of white light. The subject was instructed to blink normally and look straight ahead throughout the entire assessment. Out-in time was measured with a stopwatch and the time started immediately after the fluorescence application and stopped at the first sign of fluorescence in the post-lens tear film. The time was measured up to 5 min due to the dilution of fluorescence over time. If the time exceeded 5 min, the measurement was recorded as " > 5 min. The eye to be measured first was randomized and Out-in time was measured on both eyes with one lens type per day on three separate days for Visits 2–4. After 5-hour post-lens insertion, lens fit and assessment were evaluated by the investigator and a questionnaire was distributed to each subject to rate comfort and haziness/fogging of each eye while wearing lenses. These parameters were evaluated using a visual analog scale questionnaire. Comfort was rated on a scale from 0 to 100, where 0 was defined as "can't be worn, causes pain" and 100 as "cannot be felt." Haziness/fogging was rated on a scale from 0 to 100, where 0 was defined as "no haziness/fogging ever" and 100 as "extreme fogging."

Tear dynamics under a scleral lens for 5 h of lens wear was assessed with fluorogram in Group 2. For Visits 2–4, one of the three different pairs of scleral lenses was used per visit based on pre-determined randomization schemes. The investigator filled the bowl of the scleral lens with 0.01% w/v FITC-Dextran solution (MW = 10,000D) and inserted it into pre-determined randomized eye first. Fluorogram of the eye was collected immediately after lens insertion. The same procedure was then repeated in the other eye. High-MW FITC-Dextran solution used for fluorogram and Out-in method typically has minimal or no corneal penetration [1,13,17]. Fluorogram snapshots were obtained at time = 0–1 (immediately), 10, 20, 30, 60, 90, 120, 180, 240, and 300 min after lens insertion. The detailed procedure of our unique technique of fluorogram can be found in a previous paper [16]. To summarize, the fluorogram consisted of two parts. First, hardware was modified on a Nikon FS-2 slit lamp (Nikon Corporation, Ophthalmic Instruments Section, Tokyo, Japan). These hardware modifications were attaching a digital camera (Canon EOS 7D, Canon U.S.A., Inc., Melville, New York) to the slit-lamp biomicroscope to save the images directly to a PC, replacing the original excitation and emission filter set with a new set of filters designed for epifluorescence to get rid of any "hot spot," and enlarging the working distance to expand the illumination area. Second, to compensate for non-uniform illumination, a novel image-processing method was used by adjusting pixel fluorescence intensity based on the illumination intensity at each pixel. With image analysis, the fluorogram converted qualitative information into a quantitative measurement. The whole cornea was divided into 4 quadrants and then average intensities along each concentric arc as a function of radius were calculated. The average intensity at any given radius was calculated by summing all pixel values along the concentric arc centered on the cornea and then dividing the sum by the number of pixels along the arc of interest. This analysis indicated how fluorescence intensity varied at different locations, times, and quadrants. At each radius, there were 10 intensity data points from the aforementioned 10 measurements

during the 5-hour lens wear period. Immediately following each fluorogram snapshot, central PoLTT was measured with optical coherence tomography and a caliper tool provided by Bioptigen software. These measurements were gathered by the same observer to minimize interobserver variability. At the end of each visit, lenses were removed, ocular-surface health was assessed using slit-lamp biomicroscopy with sodium fluorescein, and exit visual acuity was measured.

2.3. Statistical analysis

Data quality and validity were assessed by checking descriptive statistics such as mean, median, standard deviation, and histogram distributions. Estimates of relationship between Out-in time and self-report variables, PoLTT were carried out by PROC MIXED, an integrated program within the SAS statistical package. The hypothesis was examined by assigning both fixed and random effects, where the potential within-subject correlations introduced by repeated measurements and paired eyes had been controlled as random effects.

3. Results

3.1. Subject demographics and lens parameters

Twenty eyes of ten neophytes (6 females; 4 Asians, 3 Caucasians, 1 Hispanics, and 2 other ethnicities) with a mean (SD) age of 22.2 (2.2) years completed the study in Group 1. Twenty eyes of ten neophytes (2 females; 4 Asians, 4 Caucasians, 2 Hispanics) with a mean (SD) age of 21.0 (2.0) years completed the study in Group 2. Table 1 reports average lens parameters and ocular features for Group 1. Tan et al. [13] reported the average lens parameters and ocular features for Group 2. All lenses in both cohorts were ordered with standard peripheral curves.

3.2. Out-in time

This study examined Out-in times at 5-hour post-lens insertion for Group 1 and compared the results obtained from a previous study [13], which measured Out-in times at 20-min post-lens insertion. 60% of Out-in measurements in Group 1 (Table 2) achieved Out-in times less than 5 min at 5-hour post-lens wear compared with 67% of Out-in measurements at 20-min post-lens wear as reported in Table 3 from Tan et al. [13]. The overall median of Out-in times was 180 s for Group 1 compared with 90 s for Group 2 from our previous study [13]. The average PoLTT for Group 1 at 5-hour post-lens insertion was 174 μ m (95% confidence interval, 165 to 183 μ m) with a range of 102 to 262 μ m. Excluding the observations with Out-in times exceeding 5 min, no association was found between Out-in times and post-lens tear thickness at 5-hour post-lens insertion ($p > 0.05$); however, our previous study observed a direct relationship between the post-lens tear thickness and Out-in times at 20-min post-lens insertion [13]. These results suggested that after 5 h of wearing time, a change in post-lens tear thickness within a range of 100 μ m to 250 μ m could not induce a significant difference in tear dynamics.

Table 1
Descriptive statistics of ocular and lens parameters for Group 1.

Variable	Mean [95% CI]
Lens base curve (mm)	7.77 [7.61, 7.93]
Lens power (D)	−3.93 [−2.84, −5.01]
Lens thickness (μ m)	422.53 [402.08, 442.97]
Ocular Sagittal height at a chord of 10 mm (μ m)	1.66 [1.63, 1.69]
Degree 0	
Ocular Sagittal height at a chord of 10 mm (μ m)	1.67 [1.65, 1.70]
Degree 180	
Horizontal visible iris diameter (mm)	11.43 [11.02, 11.85]

Table 2
Descriptive statistics of Out-in times for Group 1.

Out-in times (second)	Frequency	Percent
< 30	6	10%
30–59	10	17%
60–89	6	10%
90–119	3	5%
120–179	3	5%
180–299	8	13%
≥ 300	24	40%

Table 3
Descriptive statistics of Subjective Ratings.

Variable	Mean [95% CI]	Min	Max
Comfort	73 [70, 77]	15	100
Haziness/Fogging	23 [18, 27]	0	87
Overall			
Variable	Mean [95% CI]	Min	Max
Comfort	66 [61, 72]	15	99
Haziness/Fogging	24 [18, 31]	0	78
Group 1			
Variable	Mean [95% CI]	Min	Max
Comfort	73 [68, 78]	15	100
Haziness/Fogging	22 [17, 27]	0	87
Subjects with Out-in times < 5min			
Variable	Mean [95% CI]	Min	Max
Comfort	74 [68, 80]	27	99
Haziness/Fogging	24 [17, 31]	0	78

Subjects with Out-in times ≥ 5min.

3.3. Post-lens tear film fluorescein intensity vs. PoLTT

20 eyes from 10 subjects in Group 2 provided 60 series of data for fluorescence intensity in the post-lens tear reservoir and PoLTT changes during 5 h of lens wear at 3 separate visits. Fluorescence intensity was measured with the fluorogram method in four quadrants (superior, inferior, nasal, and temporal) at 2 mm (dashed line) and 5 mm radius (dash-dotted line) from the central cornea. PoLTT was measured with the optical coherence tomography and captured at the central cornea (solid line) and after each fluorogram snapshot. Fluorescence intensities and PoLTT changes were plotted on the same graph of each quadrant for a qualitative analysis on the tear dynamics underneath a scleral lens. The investigator labeled each visit per eye into one of the three categories: tear exchange and mixing, lens settling, and others. Fig. 1 is an example of tear exchange and mixing. The post-lens fluorescence intensity declined in this example while minimal changes in PoLTT were observed. This was primarily a result from fluorescence dilution due to predominately tear exchange and mixing. Fig. 2 is an example of lens settling. The fluorescence intensity decrease was primarily due to thinning of the tear reservoir as the fluorescence intensity curve followed the same trend as PoLTT changes. Those that were not categorized in either tear exchange and mixing or lens settling groups were classified in the “others” group. Through this qualitative analysis of 60 series of data from 20 eyes in Group 2, 13% was mostly due to tear exchange and mixing while 27% was predominately due to lens settling. The remaining 60% belonged to the “others” group, which the observed decline in fluorescence intensity was due to a combination of tear exchange, mixing and lens settling.

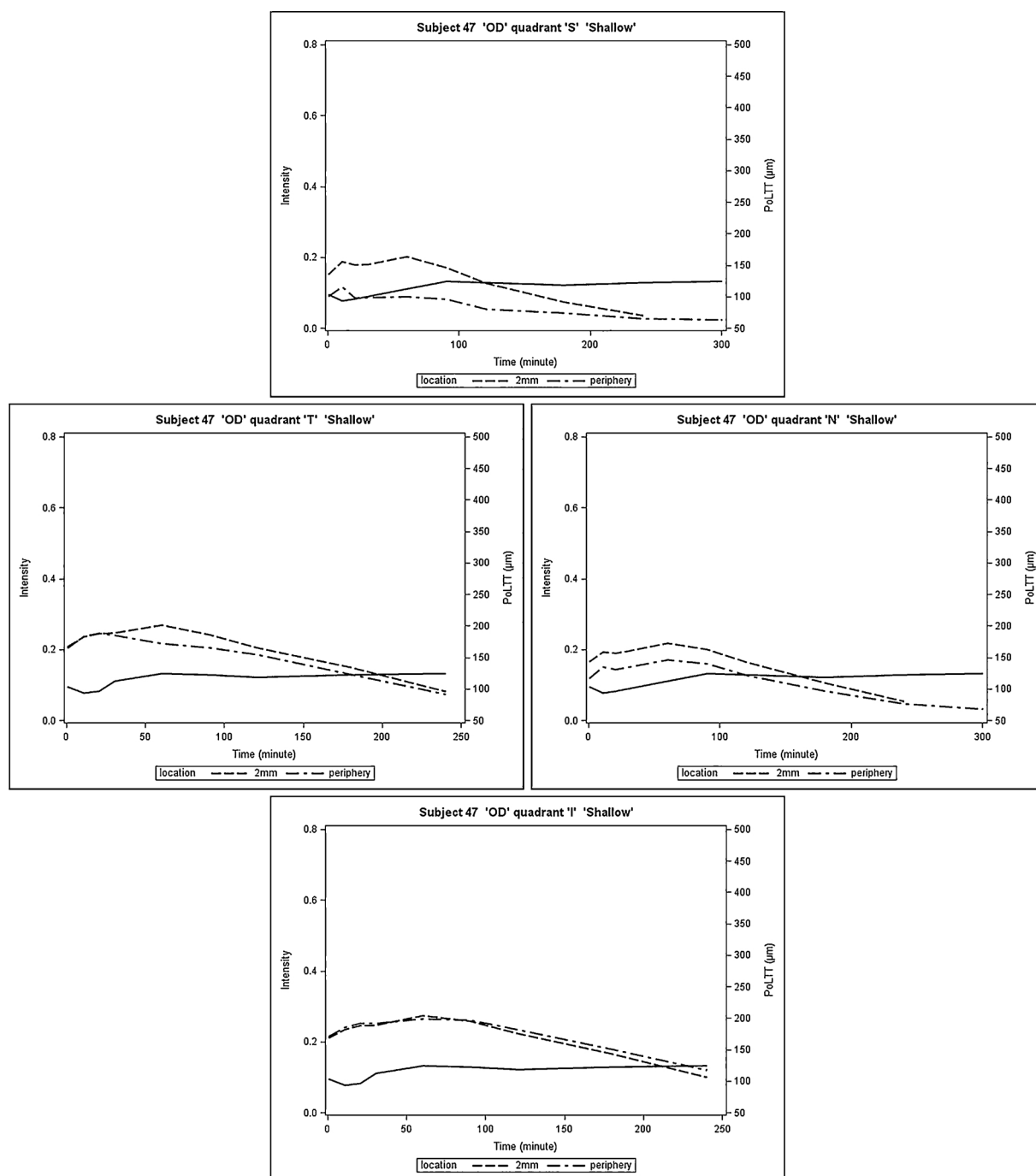


Fig. 1. Example of Tear Exchange and Mixing. Fluorescence intensity was measured in four quadrants (superior, inferior, nasal, and temporal) at 2 mm (dashed line) and 5 mm radius (dash-dotted line) from the central cornea. Post-lens Tear Thickness (solid line) was measured at the central cornea.

3.4. Subjective ratings

As shown in Table 3, the overall mean subjective rating scores reported by 20 subjects from both cohorts after 5 h of lens wear was 73 for ocular comfort (ranging from 15 to 100 where 100 was most comfortable) and was 23 for haziness/fogging (ranging from 0 to 87 where 100 was most hazy or foggy). The mean subjective rating scores for comfort and haziness/fogging were 66 and 24 for Group 1, compared with 81 and 20 from previous study [13]. For subjects with Out-in times less than 5 min, the mean subjective rating scores were 73 and 22, similar with 74 and 24 for subjects with Out-in times equal or greater than 5 min ($p > 0.05$). Out-in times at 20 min and 5 h after lens insertion were not associated with the subjective ratings for comfort and

haziness/fogging in both groups ($p > 0.05$). Low comfort score (15) was reported by one subject due to poor lens surface wettability on the anterior surface of the scleral lenses during one visit.

4. Discussion

To evaluate the presence of post-lens tear exchange during scleral lens wear, tear flow into the tear reservoir under a scleral lens was investigated in 10 healthy neophytes at 5-hour post-lens insertion and the results were compared with those obtained from a previous study using the same Out-in method. The majority (60.0%) of the subjects in Group 1 at 5-hour post-lens insertion and majority (67%) in our previous study [13] at 20-min post-lens insertion achieved Out-in times

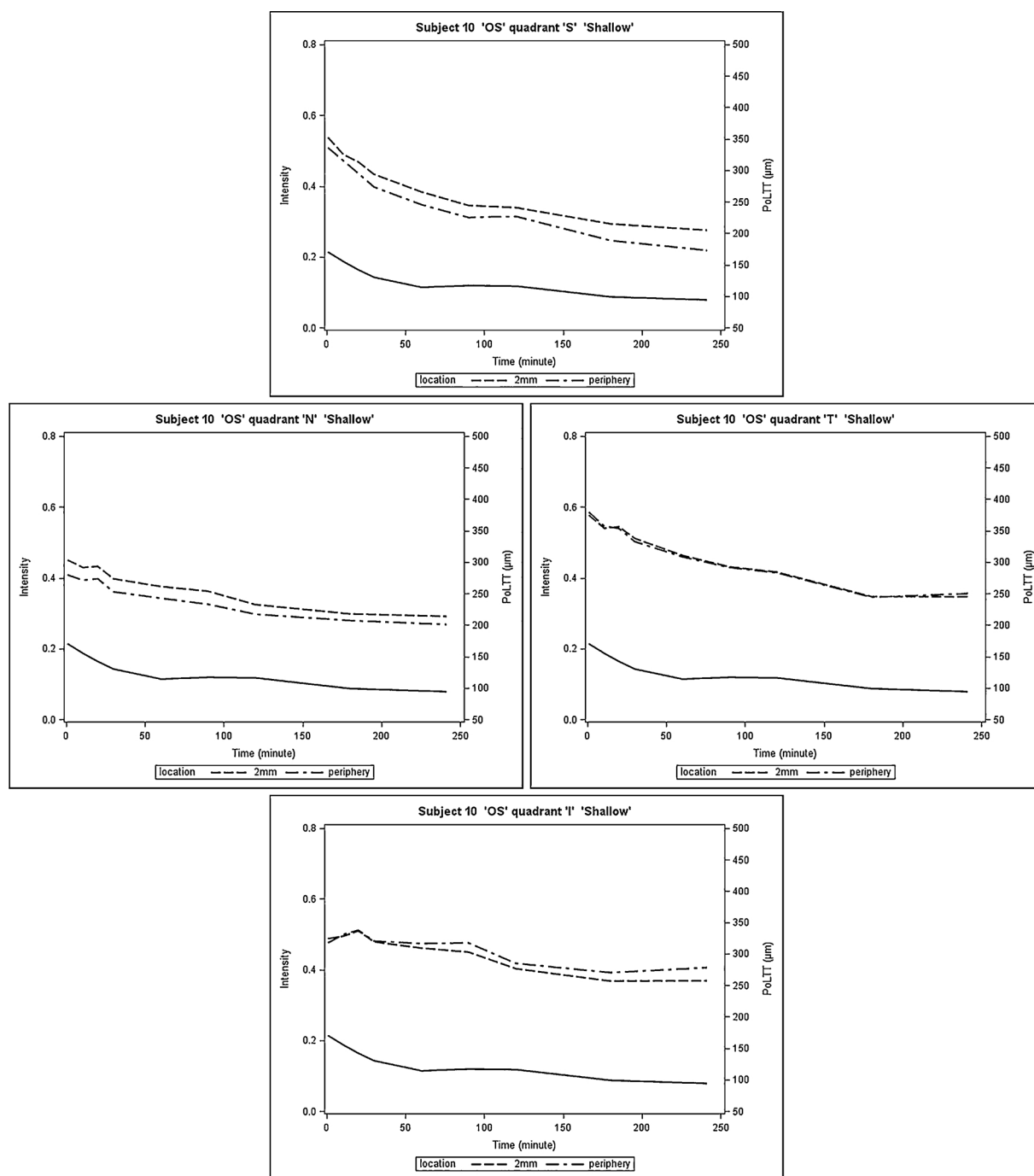


Fig. 2. Example of Lens Settling. Fluorescence intensity was measured in four quadrants (superior, inferior, nasal, and temporal) at 2 mm (dashed line) and 5 mm radius (dash-dotted line) from the central cornea. Post-lens Tear Thickness (solid line) was measured at the central cornea.

less than 5 min. Because fluorescein dye appeared in the post-lens tear reservoir under a scleral lens at two different time points during lens wear, majority of the subjects with healthy corneas continued to have tear flow into the tear reservoir after the lens had fully settled.

Other studies had assessed tear mixing under a scleral lens with fluorimetry and observed minimal tear exchange with scleral lens wear [18,19]. However the decrease in fluorescence intensity less accurately reflected the quantitative amount of tear exchange and mixing underneath a scleral lens compared with a soft contact lens and a corneal gas-permeable lens. This was because the decrease in fluorescence intensity under a scleral lens could be a combination of post-lens tear layer thinning (due to lens settling) and fluorescein concentration changes

(due to tear exchange and tear mixing). By simultaneously taking account both fluorescence intensity and post-lens tear thickness changes, as well as lens settling underneath a scleral lens to the fluorescence decay in the post-lens tear reservoir. Of interest, when the fluorogram-OCT qualitative analysis and Out-in times were compared, roughly one-third of the subjects, despite the measurement techniques, had no tear flow into the tear reservoir as the observed decline in post-lens fluorescence intensity over 5 h of lens wear was primarily due to lens settling (27%) and not to tear exchange.

In this study two methods (Out-in and fluorogram) were employed in the same cohort by examining the fluorogram-OCT qualitative

analysis in Group 2 with the Out-in times performed at 20-min post-lens insertion from our previous study [13]. 70% of Out-in times less than 5 min measured at 20-min post-lens insertion continued to have a combination of tear mixing, exchange, and lens settling over 5 h, as confirmed by fluorogram. This suggested that the majority of Out-in times performed at 20 min after lens insertion was not simply due to lens settling and many subjects with Out-in times less than 5 min continued to have tear mixing and exchange under a scleral lens as shown by fluorogram results obtained over 5 h of lens wear. Out-in method at 20 min could be a useful and convenient approach to assess tear exchange during scleral lens fitting to avoid lens seal in a clinical setting.

Post-lens tear exchange and mixing under a scleral lens might be slower than under a soft contact lens [13,19], however a direct comparison between the two lens types should be approached with caution. The initial PoLTT between the posterior lens surface and the anterior corneal surface is usually greater than 100 μm under a scleral lens and less than 10 μm under a soft contact lens. The thicker PoLTT under a scleral lens minimizes the lens-cornea interaction and creates a protective fluid layer for the cornea. Because of the scleral lens settling on the eye and thicker PoLTT, it is difficult to quantify how much tear mixing and exchange occurs under a scleral lens. Tear flow into the tear reservoir occurred in majority of the subjects during and after 5 h, but Out-in times were not associated with the post-lens tear thickness and the subjects' overall ratings for comfort and haziness/fogging. In fact, the mean subjective ratings were similar when comparing subjects who had tear flow into the tear reservoir with those who did not have tear flow within 5 min. These observations suggested that the post-lens tear reservoir did not seem to facilitate the rate of tear exchange after 5 h of lens wear and tear flow into the tear reservoir was not a significant factor that affected the subjects' symptoms of fogging and comfort during scleral lens wear. Separation of tear exchange and mixing was not possible with our methods as fluorescence intensity changes rely on both factors. Interestingly, Kim et al. [20] recently showed that there was a temperature gradient within the thick post-lens tear reservoir that could cause natural convection (or tear mixing). Their simplified model showed that tear mixing velocity had a quadratic relationship with the post-lens tear thickness (i.e., more tear mixing with thicker PoLTT) and, therefore, could potentially help supply oxygen to and remove debris from the central cornea. Therefore, further research is warranted to understand the tear mixing within the tear reservoir due to the temperature gradient and other potential mechanisms during scleral lens wear.

In conclusion, tear flow into the tear reservoir under a scleral lens on healthy subjects occurred at 20 min and at end of the 5-hour lens wear. There was roughly one-third of our study cohorts had no tear flow into the tear reservoir during lens wear as the observed decline in fluorescence intensity was predominately due to lens settling. Out-in method at 20 min could be a useful tool to assess tear exchange during scleral lens fitting, as demonstrated by comparing Out-in times with fluorogram. Out-in times were not associated with the overall subjective ratings, suggesting that tear flow into the tear reservoir might not be a contributing factor to the symptoms on fogging and comfort during scleral-lens wear. Future studies are warranted to further understand how tear flow and other potential mechanisms affect ocular health and visual qualities during scleral lens wear.

Taxonomy

Scleral Contact Lens, Ophthalmologic Instruments

Grant/financial support

Clinical Research Center Unrestricted Fund (MC Lin); Lagado Corporation for donating lens materials; Essilor USA for research fund (MC Lin)

Commercial relationship interest

None.

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